

PATENT COOPERATION TREATY

PCT

NOTIFICATION OF THE RECORDING
OF A CHANGE(PCT Rule 92bis.1 and
Administrative Instructions, Section 422)

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| Date of mailing (day/month/year) 20 November 2000 (20.11.00) |
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| Applicant's or agent's file reference 18608P WO | IMPORTANT NOTIFICATION |
| International application No. PCT/EP99/03527 | International filing date (day/month/year) 21 May 1999 (21.05.99) |

| | | |
|---|----------------------------|--------------------------|
| 1. The following indications appeared on record concerning: | | |
| <input checked="" type="checkbox"/> the applicant <input type="checkbox"/> the inventor <input type="checkbox"/> the agent <input type="checkbox"/> the common representative | | |
| Name and Address CREATOGEN GMBH Ulmer Strasse 160a D-86156 Augsburg Germany | State of Nationality DE | State of Residence DE |
| | Telephone No. | |
| | Facsimile No. | |
| | Teleprinter No. | |

| | | |
|---|----------------------------|--------------------------|
| 2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning: | | |
| <input checked="" type="checkbox"/> the person <input type="checkbox"/> the name <input type="checkbox"/> the address <input type="checkbox"/> the nationality <input type="checkbox"/> the residence | | |
| Name and Address CREATOGEN AKTIENGESELLSCHAFT Ulmer Strasse 160a D-86156 Augsburg Germany | State of Nationality DE | State of Residence DE |
| | Telephone No. | |
| | Facsimile No. | |
| | Teleprinter No. | |

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| 3. Further observations, if necessary: |
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| 4. A copy of this notification has been sent to: | |
| <input checked="" type="checkbox"/> the receiving Office <input type="checkbox"/> the International Searching Authority <input type="checkbox"/> the International Preliminary Examining Authority | <input type="checkbox"/> the designated Offices concerned <input checked="" type="checkbox"/> the elected Offices concerned <input type="checkbox"/> other: |

| | |
|---|---|
| The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No.: (41-22) 740.14.35 | Authorized officer Aino Metcalfe Telephone No.: (41-22) 338.83.38 |
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PATENT COOPERATION TREATY

18. JAN. 2001

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NOTIFICATION OF TRANSMITTAL
OF COPIES OF TRANSLATION
OF THE INTERNATIONAL PRELIMINARY
EXAMINATION REPORT
(PCT Rule 72.2)

From the INTERNATIONAL BUREAU

To:

Frist:
Patentanwälte

WEICKMANN, H.
Kopernikusstrasse 9
D-81679 München
ALLEMAGNE

| | |
|--|--|
| Date of mailing (day/month/year) 05 January 2001 (05.01.01) | |
| Applicant's or agent's file reference 18608P WO | IMPORTANT NOTIFICATION |
| International application No. PCT/EP99/03527 | International filing date (day/month/year) 21 May 1999 (21.05.99) |
| Applicant CREATOGEN AKTIENGESELLSCHAFT et al | |

1. Transmittal of the translation to the applicant.

The International Bureau transmits herewith a copy of the English translation made by the International Bureau of the international preliminary examination report established by the International Preliminary Examining Authority.

2. Transmittal of the copy of the translation to the elected Offices.

The International Bureau notifies the applicant that copies of that translation have been transmitted to the following elected Offices requiring such translation:

AU,CA,CN,JP,KP,KR,NZ,PL,US

The following elected Offices, having waived the requirement for such a transmittal at this time, will receive copies of that translation from the International Bureau only upon their request:

AP,EA,EP,AE,AL,AM,AT,AZ,BA,BB,BG,BR,BY,CH,CU,CZ,DE,DK,EE,ES,FI,GB,GD,GE,GH,GM,HR,
HU, ID, IL, IN, IS, KE, KG, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, PT, RO, RU, SD, SE,
SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, OA

3. Reminder regarding translation into (one of) the official language(s) of the elected Office(s).

The applicant is reminded that, where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report.

It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned (Rule 74.1). See Volume II of the PCT Applicant's Guide for further details.

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|---|--|
| The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland | Authorized officer Charlotte ENGER  |
| Facsimile No. (41-22) 740.14.35 | Telephone No. (41-22) 338.83.38 |

Translation

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

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|---|--|--|
| Applicant's or agent's file reference 18608P WO | FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416) | |
| International application No. PCT/EP99/03527 | International filing date (day/month/year) 21 May 1999 (21.05.99) | Priority date (day/month/year) 22 May 1998 (22.05.98) |
| International Patent Classification (IPC) or national classification and IPC C12Q 1/68 | | |
| Applicant | CREATOGEN GMBH | |

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 5 sheets, including this cover sheet.

This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of 1 sheets.

3. This report contains indications relating to the following items:

- I Basis of the report
- II Priority
- III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV Lack of unity of invention
- V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI Certain documents cited
- VII Certain defects in the international application
- VIII Certain observations on the international application

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|---|--|
| Date of submission of the demand 03 December 1999 (03.12.99) | Date of completion of this report 19 July 2000 (19.07.2000) |
| Name and mailing address of the IPEA/EP | Authorized officer |
| Facsimile No. | Telephone No. |

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/EP99/03527

I. Basis of the report

1. This report has been drawn on the basis of (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments.*):

 the international application as originally filed. the description, pages 1-61, as originally filed,
pages _____, filed with the demand,
pages _____, filed with the letter of _____,
pages _____, filed with the letter of _____ the claims, Nos. 1-45.47-52, as originally filed,
Nos. _____, as amended under Article 19,
Nos. _____, filed with the demand,
Nos. 46, filed with the letter of 17 April 2000 (17.04.2000),
Nos. _____, filed with the letter of _____ the drawings, sheets/fig 1/1, as originally filed,
sheets/fig _____, filed with the demand,
sheets/fig _____, filed with the letter of _____,
sheets/fig _____, filed with the letter of _____

2. The amendments have resulted in the cancellation of:

 the description, pages _____ the claims, Nos. _____ the drawings, sheets/fig _____

3. This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

4. Additional observations, if necessary:

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/EP99/03527

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

- the entire international application.
- claims Nos. 1-17,19-33,35-45,48,50.

because:

- the said international application, or the said claims Nos. _____ relate to the following subject matter which does not require an international preliminary examination (*specify*):

- the description, claims or drawings (*indicate particular elements below*) or said claims Nos. _____ are so unclear that no meaningful opinion could be formed (*specify*):

- the claims, or said claims Nos. 1-17,19-33,35-45,48,50 are so inadequately supported by the description that no meaningful opinion could be formed.
- no international search report has been established for said claims Nos. _____

INTERNATIONAL PRELIMINARY EXAMINATION REPORTInternational application No.
PCT/EP 99/03527**Supplemental Box**

(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: III

The present international patent application discloses a process for detecting macrolide resistance in microorganisms (preferably in *Helicobacter pylori*) by *in situ* hybridisation of oligonucleotide probes raised against mutated areas of the 23S rRNA and by subsequent fluorescence detection. The application discloses three hybridisation probes for this purpose, i.e. SEQ ID NO. 1, 2 and 3.

The application does not disclose subject matter relating to a process or a hybridisation probe for detecting another type of antibiotic resistance. Claims 1-17, 19-33, 35-45, 48 and 50 are therefore not supported by the description (PCT Article 6). The description does not disclose the invention in a manner sufficiently clear and complete for the invention to be carried out by a person skilled in the art (PCT Article 5).

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/EP 99/03527

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

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|-------------------------------|--------|-----------------------------------|-----|
| Novelty (N) | Claims | <u>18, 34, 46, 47, 49, 51, 52</u> | YES |
| | Claims | | NO |
| Inventive step (IS) | Claims | <u>18, 46, 47, 49, 51, 52</u> | YES |
| | Claims | <u>34</u> | NO |
| Industrial applicability (IA) | Claims | <u>18, 34, 46, 47, 49, 51, 52</u> | YES |
| | Claims | | NO |

2. Citations and explanations

1. Claim 34 relates to the use of an *in situ* nucleic acid hybridisation process for detecting resistance to macrolide antibiotics in microorganisms.

According to the first paragraph on page 7 of the description, the known processes for determining resistances of this type have the significant disadvantage that they are too time-consuming (generally 1-2 days). Consequently, any therapy required can only be carried out after a considerable time delay.

Several processes of this type are indicated in the description and are also disclosed in the international search report citations (e.g. Journal of Antimicrobial Chemotherapy, Vol. 40, pages 283-86; Antimicrobial Agents and Chemotherapy, Vol. 41, No. 5, 1997, pages 1162-65 and Vol. 39, No. 12, 1995, pages 2770-73; Methods in Enzymology, Vol. 164, 1968, pages 673-90).

The problem addressed by the present invention was to provide a process that can be carried out more rapidly and is more reliable.

A person skilled in the art wishing to solve this problem would take into consideration *in situ* hybridisation followed by fluorescence detection, as disclosed, for example, in the Journal of Bacteriology, Vol. 172, No. 2, 1990, pages 762-770. Moreover, this is also confirmed in lines 10-12 on page 7:

*"The further development of *in situ* hybridisation for detecting point mutations provides a pointer to the solution to identifying antibiotic resistance to bacteria quickly,...".*

The subject matter of Claim 34 therefore appears to be obvious to a person skilled in the art, and thus does not involve an inventive step (PCT Article 33(3)).

2. Claims 18, 49, 51 and 52, which relate to processes that use the special oligonucleotides as per SEQ ID Nos. 1-3 and to oligonucleotides *per se*, are considered to be novel and non-obvious (PCT Article 33(2) and (3)).
3. The subject matter of Claims 46 and 47 has also neither been disclosed nor suggested in the prior art cited in the international search report.

INTERNATIONAL PRELIMINARY EXAMINATION REPORTInternational application No.
PCT/EP 99/03527**VIII. Certain observations on the international application**

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

The expression in Claims 46 and 51 "... or contains at least one 10 nucleotide-long segment thereof" is unclear (PCT Article 6).